## Cytokine regions susceptible to protease attack identified by structural alignment with Lead mutants

## of IFN $\alpha$ -2b

CDLPQTHSLGSRRTLMLLAQMRRISLFSCLKDRHDF**GFPQEEFGNQFQK**AETIPVL**HEMIQQIFNLFSTKDSSAAWDE**TLLDKFYTELYQQLNDLEACVIQG IFN-a2b

**vgvtetplakkedsilavrkyporitlylkekk**yspcawevvraeimrsfslstnl**oeslrsk** 

Exemplary protein of the interferons/interleukin-10 family

MSYNLLGFLQRSSNFQCQKLLWQLNGRLEYCLKDRMNF<mark>DIPEEIKQLQQFQ</mark>KEDAALTI**YEMLQNIFAIFRQDSSSTGWNET**IVENLLANVYHQINHLKTVLEEK IFN-B

LEKEDPTRGKLMSSLHLKRYYGRILHYLKAKEYSHCAWTIVRVEILRNFYFINRLTGYLRN

Exemplary protein of the short-chain cytokines family

REPLACEMENT SHEET

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Title: Rational evolution of cytokines for higher stability, the cytokines and encoding nucleic acid molecules

encoding nucleic acid molecules

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APPRLICDSRVLERYLLEAKEAENITTGCAEHCSLN**ENITVPDTKVNFYAWKRMEV**GQQAVEVWQG**LALLSEAVLRGQALLVNSSQ**PWEPLQLHVDKAVSGLRSL EPO

ttllralgaqkea**isppdaasaaplrtit**adtfrklfrvysnflrgklklytgea<mark>crtgdr</mark>

Exemplary protein of the long-chain cytokines family

TPLGPASSLPQSFLLKCLEQVRK1QGDGAALQEKLVSECATYKLCHPEELVLLGHSLGI**PWAPLSSCPSQALQ**LAGCLSQL**HSGLFLYQGLLQALEGISPELG**PTLDTLQL G-CSF

DVADFATTIWQQMEEL**GMAPALQPTQGAMPAFASAF**QRRAGGVLVASHLQSFLEVSY**RVLRHLAQP** 

FIG. 9

